II. REMARKS

Upon entry of the new claims, claims 23-32 will be pending. Claims 1-22 have been cancelled herein.

A. Regarding the Amendments

Claims 1-22 are cancelled herein without disclaimer and without prejudice.

New claims 23-33 have been added. The new claims are supported, for example, by Example 1(F) at page 20, lines 1-15, and Example 2, pages 20-28. Example 1(F) describes experiments involving induction of resistance to the free radical generator paraquat in Drosophila by treatment with an inhibitor of histone deacetylase. Example 2 illustrates induction of genes by treatment with a histone deacetylase inhibitor, including genes involved in free radical or oxidative stress. Table 2 at pages 22-25, and Table 3 at page 28, illustrate genes induced by treatment with 4-phenylbutyrate according to Example 2. Claims 24-27 are supported by original claims 2-5, respectively. Claims 29-33 are further supported, for example, at page 6, lines 27-31. As such, new claims 23-33 do not add new matter.

B. Regarding the Restriction Requirement

Applicants acknowledge the election of Group I, consisting of claims 1-11, and withdrawal of claims 12-22 from consideration by the Examiner as being drawn to non-elected inventions. However, in order to focus the claims on the elected group, claims 12-22 have been cancelled herein.

C. Rejection Under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed. Claims 1-7 have been cancelled, thereby rendering the rejection moot. However, in order to be fully responsive to the Office Action, Applicants will address the rejection as to new claims 23-33.

It is acknowledged in the Office Action that the specification is enabling for extending the life span of a Drosophila by administering the histone deacetylase inhibitor 4-phenylbutyric acid. It is alleged, however, that the specification provides no guidance for subjects other than Drosophila or histone deacetylase inhibitors other than 4-phenylbutyric acid. As such, it is alleged that undue experimentation would have been required for one skilled in the art to practice the claimed methods.

However, Applicants submit, with respect to the currently claimed methods, that Drosophila is currently accepted by the scientific community as a model system that is predictive of outcomes in other organisms. For example, the specification discloses that the Drosophila is an accepted model organism for the study of disease in other organisms (see, for example, page 13, line 26, to page 14, line 16). The specification further discloses that the effects of the histone deacetylase inhibitor 4-phenylbutyric acid in Drosophila, as described in the current specification, are consistent with molecular effects of histone deacetylase inhibition in other organisms, such as yeast (see, for example, paragraph bridging pages 13 and 14). As such, Applicants assert that one skilled in the art, viewing the specification, would have recognized that the currently claimed methods, as exemplified in Drosophila, would reasonably be effective in promoting free radical resistance in cells of other organisms.

In further support of this position, Applicants point out that there is no reason to believe that the exemplified method of promoting free radical resistance of an insect cell by contacting the cell with an inhibitor of histone deacetylase would not similarly be effective with respect to other types of cells. For example, Lea et. al. (Anticancer Res. 1999 May-Jun. 19(3A): 1971-6, a copy of which is attached as Exhibit A), describe use of 4-phenylbutyrate, the same compound exemplified in the current specification, and structural analogs, to effectively inhibit histone deacetylase in several

different cell types, as well as produce the similar downstream effect of inhibiting cell growth. For example, Lea et. al. reported that 4-phenylbutyrate inhibited histone deacetylase in both mouse erythroleukemia cells and human leukemic cells inhibited growth of these cells. Lea et al. further reported that other compounds, including structural analogs of 4-phenylbutyrate, similarly inhibited histone deacetylase in such cells. Applicants point out that Lea et. al. is cited in the current specification at page 20, lines 20-23. Thus, the results reported by Lea et al. confirm that, as disclosed in the subject application, agents that inhibit histone deacetylase effectively decrease histone acetylation in multiple cell types and produce similar downstream effects. As such, it is submitted that undue experimentation would not have been required for one skilled in the art to promote free radical resistance of various types of cells and organisms containing such cells by contacting such cells with an inhibitor of histone deacetylase to increase activity of genes associated with free radical resistance selected from superoxide dismutase, cytochrome P450, and glutathione S transferase, thereby promoting free radical resistance of the cell.

In summary, the specification discloses that an inhibitor of histone deacetylase can promote free radical resistance of a cell, and exemplifies the claimed methods using the compound 4-phenylbutyrate in Drosophila cells. The Specification also teaches that Drosophila cells are a model system predictive of outcomes in other organisms. As such, it is submitted that one skilled in the art, viewing the subject application, would have known how to practice the claimed methods without undue experimentation, and further that other histone deacetylate inhibiting compounds would be effective for increasing activity of genes associated with free radical resistance in a method of the invention when used in various types of cells and organisms containing such cells. Accordingly, it is respectfully requested that the Examiner reconsider and remove the rejection of the claims under 35 U.S.C. § 112, first paragraph.

D. Prior Art Rejections

The Examiner has rejected claim 1 under 35 U.S.C. § 102(a) as being anticipated by Imai et al., Nature 403, 795-800 (2000). Applicants have cancelled Claim 1 rendering the rejection moot. However, in order to be fully responsive to the rejection, Applicants traverse and address the rejection with respect to new claims 23-32.

Rejection of a claim under 35 U.S.C. § 102(a) requires that the reference describe all of the elements and all of the limitations of the rejected claim. The current claims are directed to a method of promoting free radical resistance of a cell by contacting an inhibitor of histone deacetylase with the cell in an amount effective to increase activity of genes associated with free radical resistance selected from the group consisting of superoxide dismutase, cytochrome P450, and glutathione S transferase, thereby promoting free radical resistance of the cell. Imai et al. describe the administration of trichostatin to extend the life span of yeast. As such, the teachings of Imai et al. do not include promoting free radical resistance of a cell by the administration of a histone deacetylase in an amount effective to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase.

Therefore, Imai et al. fail to disclose each and every element of the claims as now presented. As such, Applicants respectfully request that the rejection be withdrawn.

The Examiner has rejected claims 1-5 under 35 U.S.C. § 102(b) as being anticipated by Nudelman et al., Journal of Medicinal Chemistry (abstract). Claims 1-5 have been cancelled, thereby rendering the rejection moot. In order to be fully responsive to the rejection, however, Applicants traverse and address the rejection with respect to new claims 23-32.

The rejection of a claim under 35 U.S.C. § 102(b) requires that the reference describe all of the elements and limitations of the rejected claim. Nudelman et al. describe the administration of the histone deacetylase inhibitor glycerol tributyrate as an antitumor agent, thereby extending the life span of a treated animal having a B16F0 melanoma primary cancer. However, Nudelman et al. do not teach a method of promoting free radical resistance of a cell by contacting the cell with an

inhibitor of histone deacetylase to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase, as currently claimed in the present invention.

Therefore, because Nudelman et al. fail to disclose all the elements of the currently claimed methods, withdrawal of the rejection is respectfully requested.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Acct. No. 50-1355.

Respectfully submitted,

Date: December 5, 2003

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 667-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213

Enclosure: Exhibit A